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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,423	04/05/2001	Jennifer L. Hillman	PF-0505-2-DIV	6586

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FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER
VANDERVEGT, FRANCOIS P

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,423	HILLMAN ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-21* is/are pending in the application.

4a) Of the above claim(s) *4,7,9,10,13,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,5,6,8,11,12,14-17,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of U.S. Application Serial Number 09/388,774, which is a divisional of U.S. Application Serial Number 09/074,579.

Claims 1 and 2 have been canceled.

Claims 3-21 are currently pending.

Claims 4, 7, 9, 10, 13, 18 and 19 stand as withdrawn pursuant to Applicant's election with traverse in the paper filed March 25, 2002.

Claims 3, 5-6, 8, 11-12, 14-17 and 20-21 are the subject of examination in the present Office Action.

Response to Arguments

1. In view of Applicant's response filed April 19, 2004, only the following grounds of rejection are maintained.

Claim Rejections - 35 USC § 112

2. Claims 3, 5-6, 8, 11-12, 14-17 and 20-21 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite as part of the invention an antibody which specifically binds a polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1" wherein said naturally-occurring amino acid sequence has protease inhibitor activity.

A polypeptide comprising the amino acid sequence of SEQ ID NO:1 is adequately described in the specification as-filed, thereby providing an adequate written description of an antibody which specifically binds the polypeptide of SEQ ID NO:1 or immunogenic fragments thereof.

A polypeptide comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" wherein said naturally-occurring amino acid sequence has nucleotide pyrophosphohydrolase activity is a recitation of a genus of polypeptides for which Applicant has disclosed a single species: the polypeptide of SEQ ID NO:1. The claim recites that the polypeptide to which the antibody binds is "naturally-occurring" and has a testable function of "protease inhibitor activity." The specification does not provide any description regarding the identification and protease inhibitor activity testing of other members of the "naturally-occurring" polypeptide genus related to the nucleic acid encoding SEQ ID NO:1.

However, Applicant does not appear to have provided a description of which polypeptide sequences are "naturally-occurring", even among those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1. Neither does Applicant appear to have provided a description

of how the structure of the polypeptide of SEQ ID NO:1 relates to the structure of other "naturally-occurring" polypeptides which have protease inhibitor activity, even for those polypeptides at least 90% identical to the full length of the sequence of SEQ ID NO: 1. Thus neither the common attributes of the genus nor the identifying attributes of individual species other than SEQ ID NO: 1 appear to have been described.

Additionally, there is not an adequate written description of antibodies to a protein comprising SEQ ID NO: 1 or comprising fragments of SEQ ID NO: 1, as such embodiments embrace additional amino acid sequences which are not disclosed by the instant specification and may be the actual target of antibodies to a protein "comprising" SEQ ID NO: 1.

One of skill in the art would conclude that Applicant was not in possession of the claimed genus of polypeptides comprising a "naturally-occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1" wherein said naturally-occurring amino acid sequence has protease inhibitor activity. Since Applicant does not appear to have been in possession of the genus of polypeptides to which the instantly recited antibody specifically binds; Applicant in turn does not appear to be in possession of the genus of antibodies specifically binding these polypeptides.

Therefore, only an antibody to SEQ ID NO: 1 or immunogenic fragments thereof meet the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant's arguments filed April 19, 2004 have been fully considered but they are not persuasive.

Applicant argues that the specification contains an adequate written description of the claimed invention because the specification teaches SEQ ID NO: 1 and methods by which variants that are "at least 90% identical" and having protease inhibitor activity can be identified (page 26 of response). Applicant further asserts that because the claims are directed to the antibodies, not proteins, "it is the properties of the antibodies, not the proteins they bind, which is relevant" (page 22 of response). In this Applicant is correct. However, since Applicant has only described a single protein, SEQ ID NO: 1, out of a genus of over 2.9×10^{39} different polypeptide variants that the claimed antibody can bind to. Therefore, Applicant has only demonstrated possession of antibodies that specifically bind to SEQ ID NO: 1. While these antibodies that specifically bind to SEQ ID NO: may also specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has protease inhibitor activity, Applicant has not demonstrated possession of antibodies that specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has protease inhibitor activity but DO NOT also bind SEQ ID NO: 1. Accordingly, the specification does not provide an adequate written description of the claimed genus of antibodies.

3. In view of Applicant's response filed April 19, 2004, the following ground of rejection has been modified to address the "scope" of enablement, replacing the rejection over a general lack of enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3, 5-6, 8, 11-12, 14-17 and 20-21 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies that specifically bind to SEQ ID NO: 1 or immunogenic fragments thereof, does not reasonably provide enablement for antibodies that specifically bind to polypeptides that are "naturally-occurring" variants of SEQ ID NO:1 comprising at least 90% identity to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification discloses a single working example of a polypeptide that is naturally-occurring and has at least 90% identity to SEQ ID NO: 1; namely, the polypeptide of SEQ ID NO: 1. Nevertheless, there is insufficient guidance in the specification as-filed to direct a person of skill in the art as to how to make and use antibodies to a polypeptide comprising a "naturally-occurring" amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 1 even wherein said naturally-occurring amino acid sequence has protease inhibitor activity.

However, with SEQ ID NO: 1 being a polypeptide of 942 amino acid residues, "variants" that are "at least 90% identical" encompasses polypeptides with up to at least 94 undisclosed amino acid residues, resulting in a genus of at least 94^{20} or 2.9×10^{39} different polypeptide variants. Disclosure of a single amino acid sequence (SEQ ID NO: 1) is not sufficient to enable the making of antibody to all these variants, because many of these "naturally-occurring variants" will comprise immunological epitopes not found in the single disclosed species of SEQ ID NO: 1. The Court held that, "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement" (Genentech Inc. v. Novo Nordisk A/S 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997)). While a specification does not need to disclose what is well known in the art, that rule does not excuse Applicant from providing a complete disclosure. In the instant case, while the artisan may be able to make antibodies to a given polypeptide sequence, disclosure of a single species

of a genus of over 2.9 X 10^{39} different polypeptide variants can hardly be considered complete and the enablement requirement has therefore not been met.

Applicant does not appear to have provided sufficient guidance with respect to "naturally-occurring" polypeptides and how to make and use antibodies to them. Although the specification does provide some general guidance as to how to isolate other nucleic acids related to the nucleic acid encoding SEQ ID NO: 1 (e.g., pages 40-42), it is unpredictable that other "naturally-occurring" polypeptides having protease inhibitor activity and at least 90% amino acid sequence identity to SEQ ID NO: 1 exist.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Applicant does not appear to provide sufficient guidance as to other sources of "naturally-occurring" polypeptides which are at least 90% identical to SEQ ID NO: 1 and have protease inhibitor activity. The state of the art did not recognize other "naturally-occurring" polypeptides that had protease inhibitor activity and were at least 90% identical to SEQ ID NO: 1. Even though the level of skill in the art for isolating "naturally-occurring" polypeptides encoded by nucleic acids related to the nucleic acid encoding SEQ ID NO: 1 may have been high with respect to the techniques employed, skill in the art does not render the existence of a "naturally-occurring" polypeptide predictable.

The presence of a single working example and the failure of the state of the art either at the time of filing or since to recognize other "naturally-occurring" polypeptides at least 90% identical to SEQ ID NO: 1 and having protease inhibitor activity indicates that it was highly unpredictable that additional polypeptides meeting these limitation could be isolated, particularly based on the limited guidance provided in the specification as filed. Unlike the fact pattern of In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) where the presence of a hybridoma producing an antibody having the desired properties among the many hybridomas was predictable, in the instant case it is not predictable that other "naturally-occurring" polypeptides exist. Therefore, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue with respect to other "naturally-occurring" polypeptides other than SEQ ID NO: 1.

Applicant has only described a single protein, SEQ ID NO: 1, out of a genus of over 2.9 X 10^{39} different polypeptide variants that the claimed antibody can bind to. Therefore, Applicant has only demonstrated possession of antibodies that specifically bind to SEQ ID NO: 1. While these antibodies that specifically bind to SEQ ID NO: may also specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has protease inhibitor activity, Applicant has not demonstrated

possession of antibodies that specifically bind to naturally-occurring variants that are 90% identical to SEQ ID NO: 1 and has protease inhibitor activity but DO NOT also bind SEQ ID NO: 1.

Consequently, a person of skill in the art is not enabled to make and use an antibody to a "naturally-occurring" polypeptide at least 90% identical to SEQ ID NO: 1 and having protease inhibitor activity; as encompassed by the full breadth of the claims as currently recited, irrespective of the particular form of the antibody (polyclonal, monoclonal, etc.).

Conclusion

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
June 28, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
6/28/04